

## **Remarks**

### **I. Status of the Application and Claims**

As originally filed, the present application had a total of 10 claims. In previous prosecution, all of the original claims were cancelled and replaced with claims 11-34. In addition claims 12, 13, 21 and 24 were cancelled. In the present response, claims 16-18 were cancelled and new claims 35-37 were added. Thus, the claims now pending are 11, 14, 15, 19, 20, 22, 23, and 25-37.

### **II. The Amendments**

Claim 11 was amended so that it now simply recites a process in which amino acids are isolated. Processes in which amino acids are “recovered” were moved from claim 11 to claims 35-37. In addition, claims 28 and new claim 35 require that a determination be made of the amount of amino acid recovered. Support for this and various analysis methods may be found on page 21, line 31-page 22, line 6.

These amendments do not add new matter to the application and their entry is respectfully requested.

### **III. Claim Objections**

On page 2 of the Office Action, the Examiner objects to claim 28 because of an obvious grammatical error in the phrase “process for the producing an L-amino acid.” This error has been corrected in the amended claims.

## **The Rejections**

### **I. Rejection of Claims Under 35 USC § 112, Second Paragraph**

On pages 2-3 of the Office Action, claims 11, 14-20, 22-23, 25-27 and 33 are rejected as being indefinite. The Examiner alleges that the phrase “the coding sequence of SEQ ID NO:1” is unclear. However, since this phrase has been eliminated from the amended claims herein, it is respectfully submitted that the Examiner’s rejection has been obviated.

The Examiner also alleges that the term “increased production of L-threonine” is indefinite because it is not clear what the increase has been measured against. In response, Applicant has amended claims to clarify that amino acid production is increased in bacteria mutated in their *yjgF* open reading frame relative to the same bacteria prior to mutation. Applicant submits that this should be clear, *inter alia*, from the examples, *e.g.*, Example 4, in the application.

## II. Rejection of Claims Under 35 USC § 112, First Paragraph

On pages 4-14 of the Office Action, the Examiner makes several rejections based upon the allegation that a previous amendment made by Applicant constitutes new matter. The portion of the amendment that the Examiner alleges is problematic reads: “wherein said modification results in an increased production of L-threonine.”

Applicant respectfully traverses this rejection.

Although a specification must provide support for all of the limitations in an application, it is well established that it is the concept that must be present in the specification. There is no requirement that the exact same words be used. It is Applicant’s position that it should be clear from the specification that all of the modifications described (*i.e.*, deletions, additions, transversions, etc.) were for the purpose of disrupting *yjgF* and thereby increasing the production of amino acids, with threonine being the most preferred of these amino acids.

The first paragraph in the Summary of the Invention section (page 2 of the application, lines 16-21) states that the invention is directed to a process for producing amino acids, particularly L-threonine, using microorganisms in which the *yigF* open reading frame is attenuated. The term “attenuated” is later defined as a reduction or elimination of activity or concentration of an enzyme or protein (page 2, line 31-page 3, line 2). The specification also states on page 6, lines 17-21, that attenuation, in particular elimination of the *yigF* gene or open reading frame, causes improved production of amino acids, in particular L-threonine. A description of ways in which attenuation can be accomplished begins on page 10, line 22, and there is a lengthy discussion of specific genetic modifications that can be made (page 11,

line 20-page 13, line 6). Applicant submits that it should be clear from the context in which these mutations are being described that they are being carried out to disrupt *yigF* for the purpose of improving amino acid biosynthesis. Finally, as the Examiner mentions, there is a specific experimental example that is provided that helps define what is meant by the terms used in the specification (see particularly Example 4).

Given the above considerations, Applicant respectfully submits that the concept of mutating *yigF* to eliminate its activity and to thereby increase amino acid production is present in the specification and does not constitute new matter. Moreover many different types of mutations are known in the art that can be used for accomplishing this with a very high probability of success (*e.g.*, the introduction of a stop codon early in the *yigF* sequence, the deletion of all or a large portion of the *yigF* sequence, a mutation that disrupts the *yigF* reading frame or the insertion of DNA sequence directly into *yigF*).

In addition to the rejections described above, the Examiner also rejects claims 17 and 18 based upon the written description and enablement requirements of patentability. Although, for the reasons described in previous responses, Applicant does not agree with the Examiner's assessment, in the interest of advancing prosecution in this case, these claims have been cancelled herein. It should be clear however, that the remaining claims, *e.g.*, claim 11, do not exclude processes utilizing bacteria that contain mutations in addition to those affecting *yigF*. Thus, any of the genes set forth in claims 17 and 18 may be modified in bacteria and used in a process that still falls within the scope of the remaining claims.

## **II. Rejection of Claims Under 35 USC § 103**

On pages 8-11 of the Office Action, the Examiner rejects claims 11, 14-16, 19-20, 22-23, 25 and 28-34 based upon the allegation that they are obvious in light of the combination of Volz (*Prot. Sci.* 8:24-28 (1999)) and Enos-Berlage (*J. Bacteriol.* 180:6519-6528 (1998)). Volz is cited as teaching that the function of the *E. coli yigF* gene may be determined by analysis of its crystal structure and Enos-Berlage is cited as teaching a method of phenotypically characterizing the *yigF* negative bacterial mutants by culturing the bacteria and analyzing the products made. Although the references do not specifically disclose that mutations in *yigF* affect amino acid production, the Examiner argues that changes in

production are the inherent result of the mutations. Thus, the authors have allegedly taught an improved method of amino acid production even though they do not recognize it as such.

The Examiner's argument depends upon claims encompassing the collection of a fermentation broth made by bacteria without further isolation of amino acids. Since the references that were cited do not teach any relationship between *yigF* mutation and amino acid production, they clearly would not render a process that included the isolation of amino acids from a fermentation broth obvious. Amended claims 11-27 now require such isolation and, as a consequence, Applicant submits that they should no longer be subject to the Examiner's rejection.

Claims 28-37, are directed to processes in which the fermentation product of bacteria may be merely recovered, *i.e.*, isolation of amino acids is not required. However, the claims also include a requirement that the amount of amino acid present in the recovered material be determined. Such a determination is clearly not inherent in the teachings of the cited references (to be inherent a missing element must be the necessary consequence of what is taught). Since the references do not teach a relationship between amino acid production and *yigF* mutation, a process that includes a step in which amino acid levels are determined is not obvious.

In light of the above considerations, Applicant submits that the rejection of claims under 35 USC § 103 has been overcome. It is therefore respectfully requested that this rejection be withdrawn.

### **Conclusion**

In light of the amendments and discussion above, Applicant believes that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims now pending in the application be allowed. Early notice to this effect is earnestly solicited.

If, in the opinion of the Examiner, a phone call would help to expedite the prosecution of this application, the Examiner is invited to call Applicant's undersigned attorney at (202) 419-7013.

Respectfully submitted,

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